	L #	Hits	Search Text	DBs	Time Stamp
1	L1	25	vps45 or (vessicle adj trafficking adj protein?) or (vacuolar adj protein adj sorting)	USPAT; EPO; JPO; DERWENT	2001/07/24 10:31
2	L6	17	l1 and (human or sapiens)	USPAT; EPO; JPO; DERWENT	2001/07/24 10:32

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
1	US 6239264 B1	20010529	637	Genomic DNA sequences of ashbya gossypii and uses thereof	536/23.1	435/320.1 ; 536/24.3 ; 536/24.32
2	US 6197545 B1	20010306		Genetically engineered yeast with modified signal peptidase complex	435/69.1	435/254.2 ; 435/254.21 ; 435/254.22 ; 435/254.23 ; 435/471
3	US 6143491 A	20001107		Therapeutic compositions and methods and diagnostic assays for type II diabetes involving HNF-1	435/4	435/7.21 ; 436/501 ; 436/504 ; 530/388.24 ; 530/389.2 ; 530/391.3
4	US 6124446 A	20000926		Human Vps35/Mem3-related protein	536/23.1	435/252.3 ; 435/252.33 ; 435/254.11 ; 435/254.2 ; 435/320.1 ; 435/325 ; 435/419 ; 435/69.2 ; 435/7.1 ; 536/23.2 ; 536/23.4 ; 536/23.5
5	US 6071703 A	20000606		Vesicle trafficking proteins	435/6	530/350
6	US 6020540 A	20000201		Gene encoding endochitinase	800/302	435/209 ; 435/252.3 ; 435/320.1 ; 435/418 ; 435/419 ; 536/23.1 ; 536/23.2

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
7	US 5989859 A	19991123		Vesicle trafficking proteins	435/69.1	435/252.3 ; 435/325 ; 530/350 ; 536/23.5
8	US 5965395 A	19991012		Maternally transcribed protein	435/69.1	435/320.1 ; 536/23.1 ; 536/24.1
9	US 5965707 A	19991012		Rin2, a novel inhibitor of Ras-mediated signaling	530/352	530/350
10	US 5948664 A	19990907		PI 3-kinase polypeptides	435/194	
11	US 5866351 A	19990202		CD4+ T-lymphocyte proteases and genes encoding said proteases	435/23	435/226 ; 435/975
12	US 5804412 A	19980908		Nucleic acids encoding sorting nexins and methods of using same	435/69.1	435/320.1 ; 435/325 ; 530/300 ; 530/350 ; 536/23.1
13	US 5795726 A	19980818		Methods for identifying compounds useful in treating type II diabetes	435/7.21	435/4 ; 435/6 ; 435/8 ; 536/23.5
14	US 5741689 A	19980421		Methods to inhibit serine kinase activity and to alter intersubunit binding activity of phosphatidylinositol 3-kinase, and serine kinase active sequence of the	435/194	424/139.1 ; 435/252.3 ; 435/320.1 ; 435/331 ; 435/338 ; 536/23.1 ; 536/24.1

	Document ID	Issue Date	Pages	Title	Current OR	Current XRef
15	US 5627043 A	19970506		Yeast strains used to identify inhibitors of dibasic amino acid processing endoproteases	435/23	435/224 ; 435/255.2 ; 435/41 ; 435/7.91 ; 435/942
16	US 5413914 A	19950509		Yeast assay to identify inhibitors of dibasic amino acid processing endoproteases	435/23	435/224 ; 435/7.9 ; 435/7.91 ; 435/810 ; 435/975
17	US 4690683 A	19870901		Transdermal varapamil delivery device	424/448	424/449 ; 424/486

(FILE 'HOME' ENTERED AT 10:25:14 ON 24 JUL 2001)

FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 10:26:36 ON 24 JUL 2001

L1 608 S VPS45 OR (VESSICLE (W) TRAFFICKING (W) PROTEIN#) OR (VACUOLAR
L2 85 S L1 AND (HUMAN OR SAPIENS)
L3 41 DUP REM L2 (44 DUPLICATES REMOVED)

=> log y

FROM 41 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 41 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001287519 MEDLINE
DOCUMENT NUMBER: 21192216 PubMed ID: 11134028
TITLE: TSG101/mammalian VPS23 and mammalian VPS28 interact directly and are recruited to VPS4-induced endosomes.
AUTHOR: Bishop N; Woodman P
CORPORATE SOURCE: School of Biological Sciences, University of Manchester, 2.205 Stopford Bldg., Oxford Rd., Manchester M13 9PT, United Kingdom.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Apr 13) 276 (15) 11735-42.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF316887
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

AB Class E **vacuolar protein sorting** (vps) proteins are required for appropriate sorting of receptors within the yeast endocytic pathway, and most probably function in the biogenesis of multivesicular bodies. We have identified the mammalian orthologue of Vps28p as a 221- amino acid cytosolic protein that interacts with TSG101/mammalian VPS23 to form part of a multiprotein complex. Co-immunoprecipitation and cross-linking experiments demonstrated that hVPS28 and TSG101 interact directly and that binding requires structural information within the conserved C-terminal portion of TSG101. TSG101 and hVPS28 are predominantly cytosolic. However, when endosomal vacuolization was induced by the expression of a dominant-negative mutant of another class E vps protein, **human** VPS4, a portion of both TSG101 and hVPS28 translocated to the surface of these vacuoles. We conclude that TSG101 and its interacting components are directly involved in endosomal sorting.

L3 ANSWER 2 OF 41 MEDLINE
ACCESSION NUMBER: 2001290771 MEDLINE
DOCUMENT NUMBER: 21269231 PubMed ID: 11110793
TITLE: Hrs interacts with sorting nexin 1 and regulates degradation of epidermal growth factor receptor.
AUTHOR: Chin L S; Raynor M C; Wei X; Chen H Q; Li L
CORPORATE SOURCE: Department of Pharmacology and of Cell and Molecular Physiology, Bowles Center for Alcohol Studies, School of Medicine, University of North Carolina, Chapel Hill 27599, USA.
CONTRACT NUMBER: NS37939 (NINDS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Mar 9) 276 (10) 7069-78.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF218916
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB Hepatocyte growth factor-regulated tyrosine kinase substrate (Hrs) is a mammalian homologue of yeast **vacuolar protein sorting** (Vps) protein Vps27p; however, the role of Hrs in lysosomal trafficking is unclear. Here, we report that Hrs interacts with sorting nexin 1 (SNX1), a recently identified mammalian homologue of yeast Vps5p that recognizes the lysosomal targeting code of epidermal growth factor receptor (EGFR) and participates in lysosomal trafficking of the receptor. Biochemical analyses demonstrate that Hrs and SNX1 are ubiquitous proteins that exist in both cytosolic and membrane-associated pools, and that the association of Hrs and SNX occurs on cellular membranes but not in the cytosol. Furthermore, endogenous SNX1 and Hrs form a approximately 550-kDa complex that excludes EGFR. Immunofluorescence and subcellular fractionation studies show that Hrs and SNX1 colocalize on early endosomes. By using deletion analysis, we have mapped the binding domains of Hrs and SNX1 that mediate their association. Overexpression of Hrs or its SNX1-binding domain inhibits ligand-induced degradation of EGFR, but does not affect either constitutive or

ligand-induced receptor-mediated endocytosis. These results suggest that Hrs may regulate lysosomal trafficking through its interaction with SNX1.

L3 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:519662 CAPLUS
TITLE: **Human** Vam6p promotes lysosome clustering and fusion in vivo
AUTHOR(S): Caplan, Steve; Hartnell, Lisa M.; Aguilar, Ruben C.; Naslavsky, Naava; Bonifacino, Juan S.
CORPORATE SOURCE: Cell Biology and Metabolism Branch at the National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: J. Cell Biol. (2001), 154(1), 109-121
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Regulated fusion of mammalian lysosomes is crit. to their ability to acquire both internalized and biosynthetic materials. Here, we report the identification of a novel **human** protein, hVam6p, that promotes lysosome clustering and fusion in vivo. Although hVam6p exhibits homol. to the Saccharomyces cerevisiae **vacuolar protein sorting** gene product Vam6p/Vps39p, the presence of a citron homol. (CNH) domain at the NH2 terminus is unique to the **human** protein. Overexpression of hVam6p results in massive clustering and fusion of lysosomes and late endosomes into large (2-3 .mu.m) juxtanuclear structures. This effect is reminiscent of that caused by expression of a constitutively activated Rab7. However, hVam6p exerts its effect even in the presence of a dominant-neg. Rab7, suggesting that it functions either downstream of, or in parallel to, Rab7. Data from gradient fractionation, two-hybrid, and coimmunopptn. analyses suggest that hVam6p is a homooligomer, and that its self-assembly is mediated by a clathrin heavy chain repeat domain in the middle of the protein. Both the CNH and clathrin heavy chain repeat domains are required for induction of lysosome clustering and fusion. This study implicates hVam6p as a mammalian tethering/docking factor characterized with intrinsic ability to promote lysosome fusion in vivo.

L3 ANSWER 4 OF 41 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001105250 MEDLINE
DOCUMENT NUMBER: 20556005 PubMed ID: 11102511
TITLE: **Human** orthologs of yeast **vacuolar protein sorting** proteins Vps26, 29, and 35: assembly into multimeric complexes.
AUTHOR: Haft C R; de la Luz Sierra M; Bafford R; Lesniak M A; Barr V A; Taylor S I
CORPORATE SOURCE: Diabetes Branch, National Institutes of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892-1770, USA.. carol_haft@nih.gov
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (2000 Dec) 11 (12) 4105-16.
Journal code: BAU. ISSN: 1059-1524.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF175264; GENBANK-AF175265; GENBANK-AF175266
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208
AB Sorting nexin (SNX) 1 and SNX2 are mammalian orthologs of Vps5p, a yeast protein that is a subunit of a large multimeric complex, termed the retromer complex, involved in retrograde transport of proteins from endosomes to the trans-Golgi network. We report the cloning and characterization of **human** orthologs of three additional components of the complex: Vps26p, Vps29p, and Vps35p. The close structural similarity between the yeast and **human** proteins suggests a similarity in function. We used both yeast two-hybrid assays and expression in mammalian cells to define the binding interactions among these proteins. The data suggest a model in which hVps35 serves as the core of a multimeric complex by binding directly to hVps26, hVps29, and SNX1. Deletional analyses of hVps35 demonstrate that amino acid residues 1-53 and 307-796 of hVps35 bind to the coiled coil-containing domain of SNX1. In contrast, hVps26 binds to amino acid residues 1-172 of hVps35, whereas hVps29 binds to amino acid residues 307-796 of hVps35. Furthermore, hVps35, hVps29, and hVps26 have been found in membrane-associated and cytosolic compartments. Gel filtration

chromatography of COS7 cell cytosol showed that both recombinant and endogenous hVps35, hVps29, and hVps26 coelute as a large complex (approximately 220-440 kDa). In the absence of hVps35, neither hVps26 nor hVps29 is found in the large complex. These data provide the first insights into the binding interactions among subunits of a putative mammalian retromer complex.

L3 ANSWER 5 OF 41 MEDLINE
ACCESSION NUMBER: 2001040253 MEDLINE
DOCUMENT NUMBER: 20483770 PubMed ID: 11029042
TITLE: The Doa4 deubiquitinating enzyme is functionally linked to the **vacuolar protein-sorting** and endocytic pathways.
AUTHOR: Amerik A Y; Nowak J; Swaminathan S; Hochstrasser M
CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut 06520, USA.
CONTRACT NUMBER: GM53756 (NIGMS)
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (2000 Oct) 11 (10) 3365-80. Journal code: BAU. ISSN: 1059-1524.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207

AB The Saccharomyces cerevisiae DOA4 gene encodes a deubiquitinating enzyme that is required for rapid degradation of ubiquitin-proteasome pathway substrates. Both genetic and biochemical data suggest that Doa4 acts in this pathway by facilitating ubiquitin recycling from ubiquitinated intermediates targeted to the proteasome. Here we describe the isolation of 12 spontaneous extragenic suppressors of the doa4-1 mutation; these involve seven different genes, six of which were cloned. Surprisingly, all of the cloned DID (Doa4-independent degradation) genes encode components of the **vacuolar protein-sorting** (Vps) pathway. In particular, all are class E Vps factors, which function in the maturation of a late endosome/prevacuolar compartment into multivesicular bodies that then fuse with the vacuole. Four of the six Did proteins are structurally related, suggesting an overlap in function. In wild-type and several vps strains, Doa4-green fluorescent protein displays a cytoplasmic/nuclear distribution. However, in cells lacking the Vps4/Did6 ATPase, a large fraction of Doa4-green fluorescent protein, like several other Vps factors, concentrates at the late endosome-like class E compartment adjacent to the vacuole. These results suggest an unanticipated connection between protein deubiquitination and endomembrane protein trafficking in which Doa4 acts at the late endosome/prevacuolar compartment to recover ubiquitin from ubiquitinated membrane proteins en route to the vacuole.

L3 ANSWER 6 OF 41 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001103476 MEDLINE
DOCUMENT NUMBER: 20458887 PubMed ID: 11001925
TITLE: Myotubularin, a phosphatase deficient in myotubular myopathy, acts on phosphatidylinositol 3-kinase and phosphatidylinositol 3-phosphate pathway.
AUTHOR: Blondeau F; Laporte J; Bodin S; Superti-Furga G; Payrastre B; Mandel J L
CORPORATE SOURCE: Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, 1 rue Laurent Fries, BP 163, 67404 Illkirch Cedex, CU de Strasbourg, France.
SOURCE: HUMAN MOLECULAR GENETICS, (2000 Sep 22) 9 (15) 2223-9. Journal code: BRC. ISSN: 0964-6906.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB Myotubular myopathy (MTM1) is an X-linked disease, characterized by severe neonatal hypotonia and generalized muscle weakness, with pathological features suggesting an impairment in maturation of muscle fibres. The MTM1 gene encodes a protein (myotubularin) with a phosphotyrosine phosphatase consensus. It defines a family of at least nine genes in man, including the antiphosphatase hMTMR5/Sbf1 and hMTMR2, recently found mutated in a recessive form of Charcot-Marie-Tooth disease. Myotubularin shows a dual specificity protein phosphatase activity in vitro. We have performed an in

vivo test of tyrosine phosphatase activity in Schizosaccharomyces pombe, indicating that myotubularin does not have a broad specificity tyrosine phosphatase activity. Expression of active **human** myotubularin inhibited growth of S.pombe and induced a vacuolar phenotype similar to that of mutants of the **vacuolar protein sorting** (VPS) pathway and notably of mutants of VPS34, a phosphatidylinositol 3-kinase (PI3K). In S.pombe cells deleted for the endogenous MTM homologous gene, expression of **human** myotubularin decreased the level of phosphatidylinositol 3-phosphate (PI3P). We have created a substrate trap mutant which shows relocalization to plasma membrane projections (spikes) in HeLa cells and was inactive in the S.pombe assay. This mutant, but not the wild-type or a phosphatase site mutant, was able to immunoprecipitate a VPS34 kinase activity. Wild-type myotubularin was also able to directly dephosphorylate PI3P and PI4P in vitro. Myotubularin may thus decrease PI3P levels by down-regulating PI3K activity and by directly degrading PI3P.

L3 ANSWER 7 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:125798 BIOSIS
DOCUMENT NUMBER: PREV200100125798
TITLE: The **human** leucocyte **vacuolar protein sorting** (hlVps45): Cloning, expression and localization.
AUTHOR(S): Rajasekariah, P. (1); Stanley, K. K.
CORPORATE SOURCE: (1) 19 Burraneer Avenue, St Ives, NSW, 2075 Australia
SOURCE: Cell Biology International, (2000) Vol. 24, No. 12, pp. 939. print.
Meeting Info.: 7th International Congress of Cell Biology Gold Coast, Queensland, Australia September 24-28, 2000
ISSN: 1065-6995.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 8 OF 41 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001048265 MEDLINE
DOCUMENT NUMBER: 20517226 PubMed ID: 11062004
TITLE: **Human** homologues of yeast **vacuolar protein sorting** 29 and 35.
AUTHOR: Edgar A J; Polak J M
CORPORATE SOURCE: Department of Histochemistry and Tissue Engineering Centre, Imperial College School of Medicine, London, United Kingdom.. alasdair.edgar@ic.ac.uk
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Nov 2) 277 (3) 622-30.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001214
AB In the yeast Saccharomyces cerevisiae, a membrane coat complex is required for endosome to Golgi retrograde transport. The **vacuolar protein sorting** proteins Vps29p, Vps35p, and Vps26p are required for pre-vacuolar/late endosome to Golgi retrieval of the vacuolar hydrolase receptor Vps10p. They form a cargo recognition and concentration subcomplex, termed the inner shell of the retromer coat, prior to vesicle formation by the addition of the membrane-deforming outer shell. We have cloned the **human** and murine homologues of yeast Vps29p and the **human** homologue of Vps35p. They encode 182 and 796 residue proteins, with 43 and 29% identity to their respective yeast. The 10.5 kb, 5 exon, VPS29 gene is located on chromosome 12q24 and the 29.6 kb, 17 exon, VPS35 gene is on chromosome 16. In humans, Vps29p, Vps35p, and Hbeta58, the homologue of Vps26p, may form an inner shell of the retromer coat similar to that found in yeast.

L3 ANSWER 9 OF 41 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001042077 MEDLINE
DOCUMENT NUMBER: 20517446 PubMed ID: 11062261
TITLE: Rabenosyn-5, a novel Rab5 effector, is complexed with hVPS45 and recruited to endosomes through a FYVE finger domain.
AUTHOR: Nielsen E; Christoforidis S; Uttenweiler-Joseph S; Miaczynska M; Dewitte F; Wilm M; Hoflack B; Zerial M
CORPORATE SOURCE: Max-Planck-Institute for Molecular Cell Biology and

Genetics, 01307 Dresden, Germany.
SOURCE: JOURNAL OF CELL BIOLOGY, (2000 Oct 30) 151 (3) 601-12.
Journal code: HMV. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY009133
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207

AB Rab5 regulates endocytic membrane traffic by specifically recruiting cytosolic effector proteins to their site of action on early endosomal membranes. We have characterized a new Rab5 effector complex involved in endosomal fusion events. This complex includes a novel protein, Rabenosyn-5, which, like the previously characterized Rab5 effector early endosome antigen 1 (EEA1), contains an FYVE finger domain and is recruited in a phosphatidylinositol-3-kinase-dependent fashion to early endosomes. Rabenosyn-5 is complexed to the Sec1-like protein hVPS45. hVPS45 does not interact directly with Rab5, therefore Rabenosyn-5 serves as a molecular link between hVPS45 and the Rab5 GTPase. This property suggests that Rabenosyn-5 is a closer mammalian functional homologue of yeast Vac1p than EEA1. Furthermore, although both EEA1 and Rabenosyn-5 are required for early endosomal fusion, only overexpression of Rabenosyn-5 inhibits cathepsin D processing, suggesting that the two proteins play distinct roles in endosomal trafficking. We propose that Rab5-dependent formation of membrane domains enriched in phosphatidylinositol-3-phosphate has evolved as a mechanism for the recruitment of multiple effector proteins to mammalian early endosomes, and that these domains are multifunctional, depending on the differing activities of the effector proteins recruited.

L3 ANSWER 10 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000397318 EMBASE
TITLE: Proteins of the endoplasmic-reticulum-associated degradation pathway: Domain detection and function prediction.
AUTHOR: Ponting C.P.
CORPORATE SOURCE: C.P. Ponting, MRC Functional Genetics Unit, Dept. of Human Anatomy and Genetics, University of Oxford, South Parks Road, Oxford OX1 3QX, United Kingdom.
Chris.Ponting@anat.ox.ac.uk
SOURCE: Biochemical Journal, (15 Oct 2000) 351/2 (527-535).
Refs: 57
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Sequence database searches, using iterative-profile and hidden-markov-model approaches, were used to detect hitherto-undetected homologues of proteins that regulate the endoplasmic reticulum (ER)-associated degradation pathway. The translocon-associated subunit Sec63p (Sec = secretory) was shown to contain a domain of unknown function found twice in several Brr2p-like RNA helicases (Brr2 = bad response to refrigeration 2). Additionally, Cuelp (Cue = coupling of ubiquitin conjugation to ER degradation), a yeast protein that recruits the ubiquitin-conjugating (UBC) enzyme Ubc7p to an ER-associated complex, was found to be one of a large family of putative scaffolding-domain-containing proteins that include the autocrine motility factor receptor and fungal Vpsgp (Vps = **vacuolar protein sorting**). Two other yeast translocon-associated molecules, Sec72p and Hrd3p (Hrd = 3-hydroxy-3-methylglutaryl-CoA reductase degradation), were shown to contain multiple tetratricopeptide-repeat-like sequences. From this observation it is suggested that Sec72p associates with a heat-shock protein, Hsp70, in a manner analogous to that known for Hop (Hsp70/Hsp90 organizing protein). Finally, the luminal portion of Irelp (Ire = high inositol-requiring), thought to convey the sensing function of this transmembrane kinase and endoribonuclease, was shown to contain repeats similar to those in .beta.-propeller proteins. This finding hints at the mechanism by which Irelp may sense extended unfolded proteins at the expense of compact folded molecules.

L3 ANSWER 11 OF 41 MEDLINE
ACCESSION NUMBER: 2000454475 MEDLINE
DOCUMENT NUMBER: 20334374 PubMed ID: 10873832
TITLE: Sorting in the endosomal system in yeast and animal cells.
AUTHOR: Lemmon S K; Traub L M

CORPORATE SOURCE: Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA. skl@po.cwru. edu, USA.
CONTRACT NUMBER: DK53249 (NIDDK)
GM55796 (NIGMS)
SOURCE: CURRENT OPINION IN CELL BIOLOGY, (2000 Aug) 12 (4) 457-66.
Ref: 93
Journal code: AOE; 8913428. ISSN: 0955-0674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000926

AB The endosomal system is a major membrane-sorting apparatus. New evidence reveals that novel coat proteins assist specific sorting steps and docking factors ensure the vectorial nature of trafficking in the endosomal compartment. There is also good evidence for ubiquitin regulating passage of certain proteins into multivesicular late endosomes, which mature by accumulating invaginated membrane. Lipids play a central role in this involution process, as do the class E **vacuolar protein -sorting** proteins.

L3 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:859198 CAPLUS
TITLE: Cloning and characterization of **human** VPS35 and mouse Vps35 and mapping of VPS35 to **human** chromosome 16q13-q21
AUTHOR(S): Zhang, Pingzhao; Yu, Long; Gao, Jie; Fu, Qiang; Dai, Fangyan; Zhao, Yong; Zheng, Lu; Zhao, Shouyuan
CORPORATE SOURCE: State Key Laboratory of Genetic Engineering, Institute of Genetics, School of Life Science, Fudan University, Shanghai, 200433, Peop. Rep. China
SOURCE: Genomics (2000), 70(2), 253-257
CODEN: GNMCEP; ISSN: 0888-7543
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Maintenance of different organelles in eukaryotic cells depends on sorting proteins, which ensure the proper delivery of organelle-specific proteins. The studies on yeast (Saccharomyces cerevisiae) VPS35, a hydrophilic membrane protein having a direct role in the retrieval of cargo proteins, suggest a mechanism underlying a possible lysosomal protein-sorting pathway in mammalian cells. Here, we report the isolation of **human** and mouse VPS35 cDNAs, which are 3208 and 3186 bp in length, resp. The deduced proteins of the two cDNAs, which are both composed of 796 amino acids and share 99% identity, show homol. to yeast VPS35 and other VPS35 homologues of various sources ranging from Schizosaccharomyces pombe to Drosophila melanogaster (31-56% identity and 49-71% similarity), esp. in their amino- and carboxyl-termini. The conservation of VPS35 suggests that the function of this class of protein is important. The results of Northern hybridization of **human** VPS35 in 16 tissues showed that one transcript of 3.6 kb was highly expressed in brain, heart, testis, ovary, small intestine, spleen, skeletal muscle, and placenta and expressed at moderate or low levels in other tissues. Another transcript of 3.0 kb was also expressed with proportionally lower levels than the 3.6-kb transcript in all the tissues except that the 3.0-kb transcript was not detected in brain. Mouse Vps35 was widely expressed as a 3.4-kb transcript. In addn., **human** VPS35 was assigned to **human** chromosome 16q13-q21 by radiation hybrid mapping. (c) 2000 Academic Press.

REFERENCE COUNT: 11
REFERENCE(S): (2) Hille-Rehfeld, A; Biochim Biophys Acta 1995, V1241, P177 CAPLUS
(5) Marcusson, E; Cell 1994, V77, P579 CAPLUS
(6) Nothwehr, S; Mol Biol Cell 1999, V10, P875 CAPLUS
(7) Paravicini, G; Mol Biol Cell 1992, V3, P415 CAPLUS
(8) Seaman, M; J Cell Biol 1997, V137, P79 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:581321 CAPLUS
DOCUMENT NUMBER: 134:290910
TITLE: Cloning, mapping and expression analysis of VPS33B, the **human** orthologue of rat Vps33b

AUTHOR(S): Carim, L.; Sumoy, L.; Andreu, N.; Estivill, X.; Escarceller, M.
CORPORATE SOURCE: Medical and Molecular Genetics Center, Institut de Recerca Oncologica, Hospital Duran i Reynals, L'Hospitalet de Llobregat, Barcelona, 08907, Spain
SOURCE: Cytogenet. Cell Genet. (2000), 89(1-2), 92-95
CODEN: CGCGBR; ISSN: 0301-0171
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have identified VPS33B, the **human** ortholog of rat Vps33b. VPS33B encodes a transcript of 2482 nt with an ORF of 617 amino acids and a predicted protein size of 70.6 kDa. VPS33B contains a Sec-1 domain shared with a family of proteins involved in protein sorting and vesicular trafficking. Enriched expression of VPS33B was obsd. in testis. VPS33B was positioned at chromosome 15q26.1 by radiation hybrid mapping.

REFERENCE COUNT: 11
REFERENCE(S):
(1) Altschul, S; Nucl Acids Res 1997, V25, P3389 CAPLUS
(2) Bennett, M; Cell 1993, V74, P863 CAPLUS
(3) Conibear, E; Cell 1995, V83, P513 CAPLUS
(4) Deloukas, P; Science 1998, V282, P744 CAPLUS
(5) Halachmi, N; J Neurochem 1996, V66, P889 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:492064 BIOSIS
DOCUMENT NUMBER: PREV200000492185
TITLE: Application of microarray analysis to Crohn's disease.
AUTHOR(S): Serrano, Maria-Stella (1); Liu, Zhiyun; Brown, Marilyn R.; Udall, John N., Jr.; Mannick, Elizabeth E.
CORPORATE SOURCE: (1) Pediatrics, Louisiana State University Medical Center, New Orleans, LA USA
SOURCE: JPGN, (2000) Vol. 31, No. Supplement 2, pp. S83. print.
Meeting Info.: World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition Boston, Massachusetts, USA August 05-09, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:748238 CAPLUS
DOCUMENT NUMBER: 132:963
TITLE: Protein and cDNA sequences encoding three novel **human** vesicle trafficking proteins (VTP-1, VTP-2, and VTP-3)
INVENTOR(S): Bandman, Olga; Lal, Preeti; Guegler, Karl J.; Shah, Purvi; Corley, Neil C.
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: U.S., 55 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5989859	A	19991123	US 1997-967364	19971107
US 6071703	A	20000606	US 1999-368408	19990804

PRIORITY APPLN. INFO.: US 1997-967364 19971107

AB The invention provides protein and cDNA sequences for three novel **human** vesicle trafficking proteins (VTP-1, VTP-2, and VTP-3). VTP-1 was first identified in Incyte clone 75871 from a THP-1 cell line cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. The protein is 570 amino acids in length with chem. and structural homol. to a mouse **vacuolar protein-sorting** protein (mVps45). VTP-2 was first identified in Incyte clone 2056691 from a bronchial epithelium primary cell line cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. The protein is 194 amino acids in length with chem. and structural homol. to an avian homolog of AP small chains (px19). VTP-3 was first identified in Incyte clone 3086794 from an aortic tissue cDNA library using a computer search for amino acid sequence alignments; a consensus sequence was derived from overlapping and/or extended nucleic acid sequences. The protein is 177 amino acids in length with chem. and

structural homol. to a subunit of a cow coatomer (.zeta.COP). The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also relates to the use of the provided genes and/or proteins in the diagnosis, treatment, and prevention of inflammation and disorders assocd. with cell proliferation and apoptosis.

REFERENCE COUNT: 17
REFERENCE(S):
(1) Aalto, M; Cell 1992, V68, P181 CAPLUS
(2) Adams, M; Nature 1995, V377(6547 Suppl), P3 MEDLINE
(10) Kuge, O; Journal of Cell Biology 1993, V123(6), P1727 CAPLUS
(13) Niu, S; Gene 1996, V175, P187 CAPLUS
(15) Pevsner, J; Gene 1996, V183, P7 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 41 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-430395 [36] WPIDS
DOC. NO. NON-CPI: N1999-320417
DOC. NO. CPI: C1999-126861
TITLE: New **human** Vps35/Mem3-related protein for treating lysosomal storage disease and disordered membrane transport, e.g. Tay-Sachs disease, and its antagonists for treating cancer and inflammation.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): CORLEY, N C; HILLMAN, J L; SHAH, P
PATENT ASSIGNEE(S): (INCY-N) INCYTE PHARM INC
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9935265	A1	19990715	(199936)*	EN	86

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9921017	A	19990726	(199952)	
US 6124446	A	20000926	(200051)	
EP 1044269	A1	20001018	(200053)	EN

R: BE DE ES FR GB IT NL

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9935265	A1	WO 1999-US55	19990104
AU 9921017	A	AU 1999-21017	19990104
US 6124446	A	US 1998-5180	19980108
EP 1044269	A1	EP 1999-901282	19990104
		WO 1999-US55	19990104

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9921017	A	Based on	WO 9935265
EP 1044269	A1	Based on	WO 9935265

PRIORITY APPLN. INFO: US 1998-5180 19980108
AN 1999-430395 [36] WPIDS
AB WO 9935265 A UPAB: 19990908
NOVELTY - Purified **human** Vps35/Mem3-related protein (I) with a 796 amino acid (aa) sequence (given in the specification), and its fragments, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) variants of (I) with at least 90% aa identity to (I);
(2) purified polynucleotides (II) encoding (I) or (1);
(3) polynucleotides that are complementary to, or hybridize under stringent conditions with, (II);
(4) expression vectors containing at least part of (II);
(5) host cell containing (4);
(6) recombinant production of (I) by culturing cells of (5);
(7) composition containing (I) and a carrier;
(8) purified antibody (Ab) that binds (I);
(9) purified agonists and antagonists of (I); and

(10) method for detecting (II) by hybridization with its complement, optionally after polymerase chain reaction amplification.

ACTIVITY - Anticancer; Antiinflammatory.

MECHANISM OF ACTION - (I) is probably a housekeeping protein involved in vesicular transport.

USE - (I) and its agonists are used to treat or prevent lysosomal storage diseases (e.g. Tay-Sachs or Sandhoff diseases) and disorders of membrane transport (e.g. cystinuria, renal glycosuria, juvenile pernicious anemia etc.).

(I) is also used to generate antibodies (Ab) and for drug screening.

Antagonists of (I) are used to treat or prevent a wide range of cancers and inflammatory diseases (e.g. acquired immune deficiency syndrome, Crohn's disease, arthritis, infections and many others).

Nucleic acid (II) that encodes (I) is used:

(a) for recombinant production of (I);

(b) in gene therapy;

(c) as source of antagonistic antisense, triplex-forming or ribozyme molecules;

(d) as diagnostic reagent in hybridization and/or amplification assays; and

(e) for chromosome mapping.

Ab are used:

(a) directly as therapeutic antagonists;

(b) for targeted delivery of drugs;

(c) as immunoassay reagents for diagnosis or monitoring of disease;

(d) in competitive screens for (ant)agonists; and

(e) for isolating (I) from natural sources.

Dwg.0/2

L3 ANSWER 17 OF 41 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999332720 MEDLINE
DOCUMENT NUMBER: 99332720 PubMed ID: 10404641
TITLE: Molecular cloning and characterization of a cDNA encoding the **human** leucocyte **vacuolar protein sorting** (h1Vps45).
AUTHOR: Rajasekariah P; Eyre H J; Stanley K K; Walls R S; Sutherland G R
CORPORATE SOURCE: Department of Immunology, Repatriation General Hospital, Concord, University of Sydney, NSW, Australia.. pooli@crgmail.crg.nsw.gov.au
SOURCE: INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY, (1999 Jun) 31 (6) 683-94.
Journal code: CDK; 9508482. ISSN: 1357-2725.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ133421
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990805

AB We have isolated a novel cDNA clone from **human** leucocyte cDNA library, encoding a Sec1p-like **vacuolar protein sorting** (h1Vps45) which is believed to be implicated in vesicular transportation. Although the deduced amino acid (AA) sequence of this cDNA has revealed 97% identity to other known mammalian **vacuolar protein sorting**, there is an extensive variation in nucleotide sequence in comparison to that of three previously reported **human** (hVps45), rat (rVps45) and mouse (mVps45) **vacuolar protein sorting** (**Vps45**) cDNAs [1-3]. At the nucleotide sequence level h1Vps45 demonstrated 90% homology to the hVps45 and rVps45 and 89% identity to mVps45 with no significant homology in their noncoding regions. The 2.4 Kb mRNA corresponding to the h1Vps45 clone is widely distributed in a variety of **human** tissues expressing highest levels in peripheral blood mononuclear cells (PBMC), neutrophils, heart, spleen, and testis. The chromosomal mapping studies have demonstrated that the h1Vps45 is localized to long arm of **human** chromosome 1 at q21-q22. Our data indicates that we have isolated, characterized and mapped a novel cDNA encoding h1Vps45, which may play an important role in protein trafficking as well as have clinical significance in the release of inflammatory mediators e.g. histamine, bradykinin and cytokine release.

L3 ANSWER 18 OF 41 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999287321 MEDLINE
DOCUMENT NUMBER: 99287321 PubMed ID: 10360576
TITLE: Clathrin self-assembly is mediated by a tandemly repeated superhelix.

AUTHOR: Ybe J A; Brodsky F M; Hofmann K; Lin K; Liu S H; Chen L; Earnest T N; Fletterick R J; Hwang P K
CORPORATE SOURCE: The G. W. Hooper Foundation, Department of Microbiology and Immunology, University of California San Francisco, 94143, USA.
SOURCE: NATURE, (1999 May 27) 399 (6734) 371-5.
Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1B89
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990616

AB Clathrin is a triskelion-shaped cytoplasmic protein that polymerizes into a polyhedral lattice on intracellular membranes to form protein-coated membrane vesicles. Lattice formation induces the sorting of membrane proteins during endocytosis and organelle biogenesis by interacting with membrane-associated adaptor molecules. The clathrin triskelion is a trimer of heavy-chain subunits (1,675 residues), each binding a single light-chain subunit, in the hub domain (residues 1,074-1,675). Light chains negatively modulate polymerization so that intracellular clathrin assembly is adaptor-dependent. Here we report the atomic structure, to 2.6 A resolution, of hub residues 1,210-1,516 involved in mediating spontaneous clathrin heavy-chain polymerization and light-chain association. The hub fragment folds into an elongated coil of alpha-helices, and alignment analyses reveal a 145-residue motif that is repeated seven times along the filamentous leg and appears in other proteins involved in **vacuolar protein sorting** . The resulting model provides a three-dimensional framework for understanding clathrin heavy-chain self-assembly, light-chain binding and trimerization.

L3 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:102507 CAPLUS
DOCUMENT NUMBER: 128:228299
TITLE: Retrieval of resident late-Golgi membrane proteins from the prevacuolar compartment of Saccharomyces cerevisiae is dependent on the function of Grd19p
AUTHOR(S): Voos, Wolfgang; Stevens, Tom H.
CORPORATE SOURCE: Institute of Molecular Biology, University of Oregon, Eugene, OR, 97403-1229, USA
SOURCE: J. Cell Biol. (1998), 140(3), 577-590
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The dynamic vesicle transport processes at the late-Golgi compartment of Saccharomyces cerevisiae (TGN) require dedicated mechanisms for correct localization of resident membrane proteins. In this study, we report the identification of a new gene, GRD19, involved in the localization of the model late-Golgi membrane protein A-ALP (consisting of the cytosolic domain of dipeptidyl aminopeptidase A [DPAP A] fused to the transmembrane and lumenal domains of the alk. phosphatase [ALP]), which localizes to the yeast TGN. A grd19 null mutation causes rapid mislocalization of the late-Golgi membrane proteins A-ALP and Kex2p to the vacuole. In contrast to previously identified genes involved in late-Golgi membrane protein localization, grd19 mutations cause only minor effects on **vacuolar protein sorting**. The recycling of the carboxypeptidase Y sorting receptor, Vps10p, between the TGN and the prevacuolar compartment is largely unaffected in grd19.DELTA. cells. Kinetic assays of A-ALP trafficking indicate that GRD19 is involved in the process of retrieval of A-ALP from the prevacuolar compartment. GRD19 encodes a small hydrophilic protein with a predominantly cytosolic distribution. In a yeast mutant that accumulates an exaggerated form of the prevacuolar compartment (vps27), Grd19p was obsd. to localize to this compartment. Using an in vitro binding assay, Grd19p was found to interact phys. with the cytosolic domain of DPAP A. We conclude that Grd19p is a component of the retrieval machinery that functions by direct interaction with the cytosolic tails of certain TGN membrane proteins during the sorting/budding process at the prevacuolar compartment.

L3 ANSWER 20 OF 41 MEDLINE
ACCESSION NUMBER: 1998386342 MEDLINE
DOCUMENT NUMBER: 98386342 PubMed ID: 9719873
TITLE: Protein traffic in the yeast endocytic and **vacuolar protein sorting** pathways.

AUTHOR: Wendland B; Emr S D; Riezman H
CORPORATE SOURCE: Department of Biology, Johns Hopkins University, Baltimore, MD 21218, USA.
SOURCE: CURRENT OPINION IN CELL BIOLOGY, (1998 Aug) 10 (4) 513-22. Ref: 69
Journal code: AOE; 8913428. ISSN: 0955-0674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981222

AB Endocytosis is a fundamental membrane trafficking event that occurs in all eukaryotes. The yeast Saccharomyces cerevisiae has been particularly useful in efforts to uncover novel proteins that mediate endocytosis, and many of these factors share similarity with proteins from higher eukaryotes. In the past two years, progress has centered on three major areas: modifications/signaling pathways that initiate or regulate internalization, protein complexes that are implicated in the internalization process, and factors that are involved in regulation of traffic through late endosomal compartments. As the parallels between the mechanisms employed in yeast and higher eukaryotes are further explored, new insights into the complex process of endocytosis should emerge.

L3 ANSWER 21 OF 41 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998418623 MEDLINE
DOCUMENT NUMBER: 98418623 PubMed ID: 9747851
TITLE: Molecular cloning of an Arabidopsis cDNA encoding a dynamin-like protein that is localized to plastids.
AUTHOR: Kang S G; Jin J B; Piao H L; Pih K T; Jang H J; Lim J H; Hwang I
CORPORATE SOURCE: Department of Molecular Biology, Gyeongsang National University, Chinju, Korea.
SOURCE: PLANT MOLECULAR BIOLOGY, (1998 Oct) 38 (3) 437-47.
Journal code: A6O; 9106343. ISSN: 0167-4412.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF012833
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981021
Last Updated on STN: 20000303
Entered Medline: 19981009

AB Dynamin-related proteins are high molecular weight GTPase proteins found in a variety of eukaryotic cells from yeast to **human**. They are involved in diverse biological processes that include endocytosis in animal cells and **vacuolar protein sorting** in yeast. We isolated a new gene, ADL2, that encodes a dynamin-like protein in Arabidopsis. The ADL2 cDNA is 2.68 kb in size and has an open reading frame for 809 amino acid residues with a calculated molecular mass of 90 kDa. Sequence analysis of ADL2 revealed a high degree of amino acid sequence similarity to other members of the dynamin superfamily. Among those members ADL2 was most closely related to Dnm1p of yeast and thus appears to be a member of the Vps1p subfamily. Expression studies showed that the ADL2 gene is widely expressed in various tissues with highest expression in flower tissues. In vivo targeting experiments showed that ADL2:smGFP fusion protein is localized to chloroplasts in soybean photoautroph cells. In addition experiments with deletion constructs revealed that the N-terminal 35 amino acid residues were sufficient to direct the smGFP into chloroplasts in tobacco protoplasts when expressed as a fusion protein.

L3 ANSWER 22 OF 41 MEDLINE
ACCESSION NUMBER: 1998289086 MEDLINE
DOCUMENT NUMBER: 98289086 PubMed ID: 9625693
TITLE: An Arabidopsis VPS45p homolog implicated in protein transport to the vacuole.
AUTHOR: Bassham D C; Raikhel N V
CORPORATE SOURCE: Michigan State University-Department of Energy Plant Research Laboratory, Michigan State University, East Lansing, Michigan 48824-1312, USA.
SOURCE: PLANT PHYSIOLOGY, (1998 Jun) 117 (2) 407-15.
Journal code: P98; 0401224. ISSN: 0032-0889.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF036234
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811
Last Updated on STN: 20000303
Entered Medline: 19980727

AB The Sec1p family of proteins is required for vesicle-mediated protein trafficking between various organelles of the endomembrane system. This family includes Vps45p, which is required for transport to the vacuole in yeast (Saccharomyces cerevisiae). We have isolated a cDNA encoding a **VPS45** homolog from Arabidopsis thaliana (AtVPS45). The cDNA is able to complement both the temperature-sensitive growth defect and the vacuolar-targeting defect of a yeast **vps45** mutant, indicating that the two proteins are functionally related. AtVPS45p is a peripheral membrane protein that associates with microsomal membranes. Sucrose-density gradient fractionation demonstrated that AtVPS45p co-fractionates with AtELP, a potential **vacuolar protein sorting** receptor, implying that they may reside on the same membrane populations. These results indicate that AtVPS45p is likely to function in the transport of proteins to the vacuole in plants.

L3 ANSWER 23 OF 41 MEDLINE
ACCESSION NUMBER: 1998096598 MEDLINE
DOCUMENT NUMBER: 98096598 PubMed ID: 9434958
TITLE: Genetic mapping of **vacuolar protein sorting**-45 (**Vps45**) on mouse chromosome 3.
AUTHOR: Mishra V S; Holt S M; Teodoro J M; Kingsmore S F
CORPORATE SOURCE: Department of Medicine, University of Florida, Gainesville 32610-0221, USA.
CONTRACT NUMBER: AI39651 (NIAID)
SOURCE: MAMMALIAN GENOME, (1998 Jan) 9 (1) 90-1.
Journal code: BES; 9100916. ISSN: 0938-8990.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U66865
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980226

L3 ANSWER 24 OF 41 MEDLINE
ACCESSION NUMBER: 97197782 MEDLINE
DOCUMENT NUMBER: 97197782 PubMed ID: 9045632
TITLE: Identification of a mammalian Golgi Sec1p-like protein, mVps45.
AUTHOR: Tellam J T; James D E; Stevens T H; Piper R C
CORPORATE SOURCE: Center for Molecular Biology, University of Queensland, Brisbane 4072, Australia.
CONTRACT NUMBER: GM16601-01 (NIGMS)
GM32448 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Mar 7) 272 (10) 6187-93.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970424
Last Updated on STN: 19980206
Entered Medline: 19970414

AB Our understanding of lysosomal biogenesis and general vesicular transport in animal cells has been greatly enhanced by studies of vacuolar biogenesis in yeast. Genetic screens have identified a number of proteins that play direct roles in the proper sorting of vacuolar hydrolases. These include t-SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) proteins and Sec1p-like proteins, which have recently been implicated as key regulators of vesicle fusion. In this study we have extended these observations in yeast and have isolated and characterized a novel member of the Sec1p-like family of proteins from mammalian cells, mVps45. mVps45 shares a high level of identity with the Saccharomyces cerevisiae Sec1p-like protein Vps45p that is believed to function with the t-SNARE Pep12p in the fusion of Golgi-derived transport vesicles with a prevacuolar compartment. We found that mVps45 is a ubiquitously expressed peripheral membrane protein that localized to perinuclear Golgi-like and

trans-Golgi network compartments in Chinese hamster ovary cells. We found that mVps45 could bind specifically to yeast Pep12p and to the mammalian Pep12p-like protein, syntaxin 6, in vitro.

L3 ANSWER 25 OF 41 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998039459 MEDLINE
DOCUMENT NUMBER: 98039459 PubMed ID: 9372190
TITLE: Cloning and characterization of a dominant-negative vps1 allele of the yeast Saccharomyces cerevisiae.
AUTHOR: Finken-Eigen M; Muller S; Kohrer K
CORPORATE SOURCE: Biologisch-Medizinisches Forschungszentrum, Heinrich-Heine-Universitat Dusseldorf, Germany.
SOURCE: BIOLOGICAL CHEMISTRY, (1997 Oct) 378 (10) 1187-91. Journal code: CK4; 9700112. ISSN: 1431-6730.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X65124
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 20000303
Entered Medline: 19980114

AB The gene product of the yeast VPS1 gene is a member of a family of high-molecular-weight GTP-binding proteins that are involved in diverse cellular processes. The Vps1 protein (Vps1p) was shown to perform an essential function in the yeast secretory pathway. Here, we report the isolation and characterization of a mutant allele of the VPS1 gene, causing a dominant-negative **vacuolar protein sorting** (vps) defect, as demonstrated by the mislocalization of the vacuolar hydrolase carboxypeptidase Y (CPY). DNA sequence analysis of the mutant vps1 allele (vps1d-293) revealed a single point mutation, resulting in an amino acid exchange at position 293 from Ala to Asp. The mutation is located downstream of the tripartite GTP-binding motif found in the amino-terminal half of the protein. The observation that expression of wild-type Vps1p partially suppressed the dominant-negative CPY sorting phenotype indicates competition of a non-functional mutant Vps1 protein and a functional wild-type VPS1p for a Vps1p-binding site of an as yet unknown **vacuolar protein sorting** factor.

L3 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:345728 CAPLUS
DOCUMENT NUMBER: 127:61393
TITLE: The yeast VPS5/GRD2 gene encodes a sorting nexin-1-like protein required for localizing membrane proteins to the late Golgi
AUTHOR(S): Nothwehr, Steven F.; Hindes, Anna E.
CORPORATE SOURCE: Division of Biological Sciences, University of Missouri, Columbia, MO, 65211, USA
SOURCE: J. Cell Sci. (1997), 110(9), 1063-1072
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genetic anal. of late Golgi membrane protein localization in Saccharomyces cerevisiae has uncovered a large no. of genes (called GRD) that are required for retention of A-ALP, a model late Golgi membrane protein. Here we describe one of the GRD genes, VPS5/GRD2, that encodes a hydrophilic protein similar to **human** sorting nexin-1, a protein involved in trafficking of the epidermal growth factor receptor. In yeast cells contg. a vps5 null mutation the late Golgi membrane proteins A-ALP and Kex2p were rapidly mislocalized to the vacuolar membrane. A-ALP was delivered to the vacuole in vps5 mutants in a manner independent of a block in the early endocytic pathway. Null mutants vps5 also exhibited defects in both vacuolar morphol. and in sorting of a sol. vacuolar protein, carboxypeptidase Y. The latter defect is apparently due to an inability to localize the carboxypeptidase Y sorting receptor, Vps10p, to the Golgi since it is rapidly degraded in the vacuole in vps5 mutants. Fractionation studies indicate that Vps5p is distributed between a free cytosolic pool and a particulate fraction contg. Golgi, transport vesicles, and possibly endosomes, but lacking vacuolar membranes. Immunofluorescence microscopy expts. show that the membrane-assocd. pool of Vps5p localizes to an endosome-like organelle that accumulates in the class E vps27 mutant. These results support a model in which Vps5p is required for retrieval of membrane proteins from a prevacuolar/late endosomal compartment back to the late Golgi app.

L3 ANSWER 27 OF 41 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 97301565 MEDLINE

DOCUMENT NUMBER: 97301565 PubMed ID: 9157966
TITLE: A novel mosaic protein containing LDL receptor elements is highly conserved in humans and chickens.
AUTHOR: Morwald S; Yamazaki H; Bujo H; Kusunoki J; Kanaki T; Seimiya K; Morisaki N; Nimpf J; Schneider W J; Saito Y
CORPORATE SOURCE: Department of Molecular Genetics, Biocenter and University of Vienna, Austria.
SOURCE: ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1997 May) 17 (5) 996-1002.
Journal code: B89; 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y08109; GENBANK-Y08110
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19990129
Entered Medline: 19970612

AB Certain receptors belonging to the LDL receptor (LDLR) gene family appear to constitute a newly identified branch whose members are expressed in brain, in addition to other tissues. In support of this concept, we have now discovered the expression and delineated the molecular structures of a representative of this emerging branch from two such diverse species as **human** and chicken. This membrane receptor, called LR11 and thus far only known to exist in the rabbit, is a complex seven-domain mosaic protein containing, among other structural elements, a cluster of 11 LDLR ligand-binding repeats and a domain with homology to VPS10, a yeast receptor for **vacuolar protein sorting**. Cytoplasmic signature sequences define the receptor as competent for endocytosis. The most striking properties of LR11s are their (1) high degree of structural conservation (>80% identity among mammals and birds), with 100% identity in the membrane-spanning and cytoplasmic domains of rabbit and **human**; (2) lack of regulation by cholesterol and estrogen; and (3) expression in brain. The features of LR11 suggest important roles in intercellular and intracellular ligand transport processes, some of which it may share with other brain-specific LDLR family members.

L3 ANSWER 28 OF 41 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97258867 MEDLINE
DOCUMENT NUMBER: 97258867 PubMed ID: 9105038
TITLE: Endosome to Golgi retrieval of the **vacuolar protein sorting** receptor, Vps10p, requires the function of the VPS29, VPS30, and VPS35 gene products.
AUTHOR: Seaman M N; Marcusson E G; Cereghino J L; Emr S D
CORPORATE SOURCE: Division of Cellular and Molecular Medicine, University of California, San Diego, School of Medicine, La Jolla 92093-0668, USA.
CONTRACT NUMBER: GM15638 (NIGMS)
GM32703 (NIGMS)
SOURCE: JOURNAL OF CELL BIOLOGY, (1997 Apr 7) 137 (1) 79-92.
Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U10400; GENBANK-U43503
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19970514
Entered Medline: 19970508

AB Mutations in the S. cerevisiae VPS29 and VPS30 genes lead to a selective protein sorting defect in which the vacuolar protein carboxypeptidase Y (CPY) is missorted and secreted from the cell, while other soluble vacuolar hydrolases like proteinase A (PrA) are delivered to the vacuole. This phenotype is similar to that seen in cells with mutations in the previously characterized VPS10 and VPS35 genes. Vps10p is a late Golgi transmembrane protein that acts as the sorting receptor for soluble vacuolar hydrolases like CPY and PrA, while Vps35p is a peripheral membrane protein which cofractionates with membranes enriched in Vps10p. The sequences of the VPS29, VPS30, and VPS35 genes do not yet give any clues to the functions of their products. Each is predicted to encode a hydrophilic protein with homologues in the **human** and C. elegans genomes. Interestingly, mutations in the VPS29, VPS30, or VPS35 genes change the subcellular distribution of the Vps10 protein, resulting in a shift of Vps10p from the Golgi to the vacuolar membrane. The route that Vps10p takes to reach the vacuole in a vps35 mutant does not depend upon

Sec1p mediated arrival at the plasma membrane but does require the activity of the pre-vacuolar endosomal t-SNARE, Pep12p. A temperature conditional allele of the VPS35 gene was generated and has been found to cause missorting/secretion of CPY and also Vps10p to mislocalize to a vacuolar membrane fraction at the nonpermissive temperature. Vps35p continues to cofractionate with Vps10p in vps29 mutants, suggesting that Vps10p and Vps35p may directly interact. Together, the data indicate that the VPS29, VPS30, and VPS35 gene products are required for the normal recycling of Vps10p from the prevacuolar endosome back to the Golgi where it can initiate additional rounds of vacuolar hydrolase sorting.

L3 ANSWER 29 OF 41 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1998242652 MEDLINE
DOCUMENT NUMBER: 98242652 PubMed ID: 9583350
TITLE: A novel member of the LDL receptor gene family with eleven binding repeats is structurally related to neural adhesion molecules and a yeast **vacuolar protein sorting** receptor.
AUTHOR: Yamazaki H; Bujo H; Saito Y
CORPORATE SOURCE: Second Department of Internal Medicine, Chiba University School of Medicine, Japan.
SOURCE: JOURNAL OF ATHEROSCLEROSIS AND THROMBOSIS, (1997) 4 (1) 20-6. Ref: 52
Journal code: CWC; 9506298. ISSN: 1340-3478.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980610

AB We now have discovered and characterized a novel multi-domain protein and classified it as a member of the LDL receptor gene family. The approximately 250 kDa membrane protein, termed LR11, highly conserved in man, rabbit and chicken, contains a cluster of 11 LDL receptor ligand binding repeats, a group of 5 LDL receptor "YWTD" repeats, a large hexarepeat domain of structural elements found in neural cell adhesion molecules, and a domain with similarity to a yeast receptor for **vacuolar protein sorting**, VPS10. The cytoplasmic domain exhibits features typical of endocytosis-competent coated pit receptors. The mosaic, and presumably multifunctional, receptor is expressed abundantly in brain, liver and adrenal glands. Ligand blotting of LR11-transfected cells demonstrated that LR11 binds apolipoproteinE-containing lipoproteins, as well as other members of LDL receptor gene family. In contrast to the LDL receptor, the mRNA levels in rabbit liver is unaffected by hyperlipidemia. The features of this highly conserved and complex mosaic protein suggest the importance of the ever expanding LDL receptor gene family in the evolution and proposed multifunctionality.

L3 ANSWER 30 OF 41 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 97094912 MEDLINE
DOCUMENT NUMBER: 97094912 PubMed ID: 8940146
TITLE: Molecular characterization of a novel **human** hybrid-type receptor that binds the alpha2-macroglobulin receptor-associated protein.
AUTHOR: Jacobsen L; Madsen P; Moestrup S K; Lund A H; Tommerup N; Nykjaer A; Sottrup-Jensen L; Gliemann J; Petersen C M
CORPORATE SOURCE: Department of Medical Biochemistry, University of Aarhus, DK-8000 Aarhus C, Denmark.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 6) 271 (49) 31379-83.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U60975
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970109

AB The 39-40-kDa receptor-associated protein (RAP) binds to the members of the low density lipoprotein receptor gene family and functions as a specialized endoplasmic reticulum/Golgi chaperone. Using RAP affinity chromatography, we have purified a novel approximately 250-kDa brain

protein and isolated the corresponding cDNA. The gene, designated SORL1, maps to chromosome 11q 23/24 and encodes a 2214-residue type 1 receptor containing a furin cleavage site immediately preceding the N terminus determined in the purified protein. The receptor, designated sorLA-1, has a short cytoplasmic tail containing a tyrosine-based internalization signal and a large external part containing (from the N-terminal): 1) a segment homologous to domains in the yeast **vacuolar protein sorting** 10 protein, Vps10p, that binds carboxypeptidase Y, 2) five tandemly arranged YWTD repeats and a cluster of 11 class A repeats characteristic of the low density lipoprotein receptor gene family receptors, and 3) six tandemly arranged fibronectin type III repeats also found in certain neural adhesion proteins. sorLA-1 may therefore be classified as a hybrid receptor. Northern blotting revealed specific mRNA transcripts in brain, spinal cord, and testis but not in several major organs. Both RAP and an antibody against a synthetic peptide derived from a sequence determined in the mature protein detected sorLA-1 in crude **human** brain extracts. The domain structure suggests that sorLA-1 is an endocytic receptor possibly implicated in the uptake of lipoproteins and of proteases.

L3 ANSWER 31 OF 41 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 96189119 MEDLINE
DOCUMENT NUMBER: 96189119 PubMed ID: 8628304
TITLE: A yeast protein related to a mammalian Ras-binding protein, Vps9p, is required for localization of vacuolar proteins.
AUTHOR: Burd C G; Mustol P A; Schu P V; Emr S D
CORPORATE SOURCE: Division of Cellular and Molecular Medicine and Howard Hughes Medical Institute, University of California, San Diego, La Jolla, 92093-0668, USA.
CONTRACT NUMBER: GM32703 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1996 May) 16 (5) 2369-77. Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U50142
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19960708
Entered Medline: 19960621

AB In the yeast Saccharomyces cerevisiae, mutations in **vacuolar protein sorting** (VPS) genes result in secretion of proteins normally localized to the vacuole. Characterization of the VPS pathway has provided considerable insight into mechanisms of protein sorting and vesicle-mediated intracellular transport. We have cloned VPS9 by complementation of the **vacuolar protein sorting** defect of vps9 cells, characterized its gene product, and investigated its role in **vacuolar protein sorting**. Cells with a vps9 disruption exhibit severe **vacuolar protein sorting** defects and a temperature-sensitive growth defect at 38 degrees C. Electron microscopic examination of delta vps9 cells revealed the appearance of novel reticular membrane structures as well as an accumulation of 40- to 50-nm-diameter vesicles, suggesting that Vps9p may be required for the consumption of transport vesicles containing vacuolar protein precursors. A temperature-conditional allele of vps9 was constructed and used to investigate the function of Vps9p. Immediately upon shifting of temperature-conditional vps9 cells to the nonpermissive temperature, newly synthesized carboxypeptidase Y was secreted, indicating that Vps9p function is directly required in the VPS pathway. Antibodies raised against Vps9p immunoprecipitate a rare 52-kDa protein that fractionates with cytosolic proteins following cell lysis and centrifugation. Analysis of the VPS9 DNA sequence predicts that Vps9p is related to **human** proteins that bind Ras and negatively regulate Ras-mediated signaling. We term the related regions of Vps9p and these Ras-binding proteins a GTPase binding homology domain and suggest that it defines a family of proteins that bind monomeric GTPases. Vps9p may bind and serve as an effector of a rab GTPase, like Vps21p, required for **vacuolar protein sorting**.

L3 ANSWER 32 OF 41 MEDLINE
ACCESSION NUMBER: 96365669 MEDLINE
DOCUMENT NUMBER: 96365669 PubMed ID: 8769846
TITLE: The Sec1 family: a novel family of proteins involved in synaptic transmission and general secretion.
AUTHOR: Halachmi N; Lev Z
CORPORATE SOURCE: Department of Biology, Technion-Israel Institute of Technology, Haifa, Israel.

SOURCE: JOURNAL OF NEUROCHEMISTRY, (1996 Mar) 66 (3) 889-97. Ref: 51
Journal code: JAV; 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970107

AB The Sec1 family, a novel family of proteins involved in synaptic transmission and general secretion, is described. To date, 14 members of this family have been identified: four yeast proteins, Sec1, Sly1, Slp1/Vps33, and **Vps45**/Stt10; three nematode proteins, Unc-18 and the homologues of Sly1 and Slp1; the Drosophila Rop; and six mammalian proteins, the rat Munc-18/n-Sec1/rbSec1A and rbSec1B, the mouse Munc-18b/muSec1 and Munc-18c, and the bovine Munc-18 and mSec1. The mammalian proteins share 44-63% sequence identity with the nematode Unc-18 and Drosophila Rop proteins and 20-29% with the yeast proteins and their nematode homologues. The Sec1 proteins are mostly hydrophilic and lack a transmembrane domain. Nevertheless, Sec1 proteins are found as membrane-bound proteins. Some of them are also found as soluble, cytoplasmic proteins. Binding of the rat brain Sec1 to the presynaptic membrane may be due to strong interaction with syntaxin, an integral component of this membrane. The rat brain Sec1 is also bound to Cdk5, a neural cyclin-dependent kinase. The Sec1 proteins play a positive role in exocytosis. Loss of function mutations in SEC1, SLY1, or SLP1 result in blocking of protein transport between distinct yeast sub-cellular compartments. Inactivation of unc-18 and rop results in inhibition of neurotransmitter release and, in the case of rop, inhibition of general secretion as well. In addition, studies of Rop and n-Sec1 indicate that they also play a negative role in synaptic transmission, mediated by their interaction with syntaxin. A working model addressing the dual regulative role of the Sec1 proteins in secretion is presented.

L3 ANSWER 33 OF 41 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 96327632 MEDLINE
DOCUMENT NUMBER: 96327632 PubMed ID: 8678978
TITLE: Genetic mapping and embryonic expression of a novel, maternally transcribed gene Mem3.
AUTHOR: Hwang S; Benjamin L E; Oh B; Rothstein J L; Ackerman S L; Beddington R S; Solter D; Knowles B B
CORPORATE SOURCE: Jackson Laboratory, 600 Main Street, Bar Harbor, Maine 04609, USA.
CONTRACT NUMBER: P30 CA34196 (NCI)
RO1 CA37225 (NCI)
SOURCE: MAMMALIAN GENOME, (1996 Aug) 7 (8) 586-90.
Journal code: BES; 9100916. ISSN: 0938-8990.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U47024
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961017

AB To study the molecular function of genes expressed during preimplantation development, we isolated a novel maternal transcript SSEC (Stage Specific Embryonic cDNA)-26 from a partial subtraction library of mouse unfertilized eggs and preimplantation embryos. The SSEC-26 transcript is abundant in the unfertilized egg and also actively transcribed from the newly formed zygotic genome. On the basis of its expression in eggs and embryos, this new mouse gene is named Mem (maternal-embryonic) 3. The genomic locus of Mem3 has been mapped to Chromosome (Chr) 8 near the D8Mit78 marker and the glutaryl CoA dehydrogenase (Gcdh) locus. The deduced amino acid sequence of MEM3 resembles that of the yeast VPS (**Vacuolar Protein Sorting**) 35 in two separate domains. A cDNA sequence of the potential **human** homolog of Mem3 has been assembled with partial clones from the EST database and assigned to **human** Chr 16.

L3 ANSWER 34 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:95859 BIOSIS
DOCUMENT NUMBER: PREV199799395062
TITLE: Molecular identification of a novel **human**

candidate **vacuolar protein sorting** receptor.
AUTHOR(S): Petersen, C. M.; Nielsen, M. S.; Nykjaer, A.; Jacobsen, L.; Rasmussen, H. H.; Rojgaard, H.; Gilemann, J.; Madsen, P.; Moestrup, S. K.
CORPORATE SOURCE: Dep. Med. Biochem., Univ. Aarhus, Aarhus 8000 C Denmark
SOURCE: Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL., pp. 267A.
Meeting Info.: Annual Meeting of the 6th International Congress on Cell Biology and the 36th American Society for Cell Biology San Francisco, California, USA December 7-11, 1996
ISSN: 1059-1524.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L3 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:77494 CAPLUS
DOCUMENT NUMBER: 126:127255
TITLE: Molecular mechanisms of neurotransmitter and neuropeptide release
AUTHOR(S): Pevsner, J.
CORPORATE SOURCE: Department of Neuroscience, The Johns Hopkins School of Medicine and Department of Neurology, The Kennedy Krieger Institute, Baltimore, MD, 21205, USA
SOURCE: Peptidergic Neuron, [Int. Symp. Neurosecretion], 12th (1996), Meeting Date 1995, 55-72. Editor(s): Krisch, Brigitte; Mentlein, Rolf. Birkhaeuser: Basel, Switz. CODEN: 63XVA3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In synaptic transmission, calcium entry into the presynaptic nerve terminal causes docked synaptic vesicles to fuse with the plasma membrane and release their neurotransmitter contents across the synapse. A biochem. pathway for synaptic vesicle docking and fusion is currently being elucidated. The proteins implicated in this pathway are conserved between eukaryotes from yeast to mammals, and isoforms of these proteins mediate vesicle trafficking in a variety of constitutive and regulated transport steps. It is likely that the mol. mechanisms of synaptic vesicle exocytosis also apply to the release of neuropeptides from large dense-core vesicles. The authors have characterized n-sec 1, a cytosolic protein of the nerve terminal that binds syntaxin. The authors have also identified three mammalian homologs of n-sec 1 that may regulate vesicle trafficking between the Golgi app. and lysosomes.

L3 ANSWER 36 OF 41 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 97149272 MEDLINE
DOCUMENT NUMBER: 97149272 PubMed ID: 8996080
TITLE: Mammalian homologues of yeast **vacuolar protein sorting** (vps) genes implicated in Golgi-to-lysosome trafficking.
AUTHOR: Pevsner J; Hsu S C; Hyde P S; Scheller R H
CORPORATE SOURCE: Beckman Center, Stanford University Medical School, CA 94305, USA.
SOURCE: GENE, (1996 Dec 12) 183 (1-2) 7-14.
Journal code: FOP; 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U35244; GENBANK-U35245; GENBANK-U35246
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19980206
Entered Medline: 19970213
AB Sec1p, Vps33p, Vps45p and Sly1p constitute a family of proteins implicated in vesicle trafficking at distinct stages of the yeast secretory pathway. Several mammalian homologues of Sec1p have been described, including n-sec1 which has been implicated in the regulation of synaptic vesicle docking at the nerve terminal. We have characterized cDNA clones encoding three additional mammalian homologues belonging to this family: r-vps33a and r-vps33b from rat, which are 30 and 26% identical to yeast Vps33p, respectively, and h-**vps45** from **human** which is 38% identical to yeast Vps45p at the amino acid (aa) level. Phylogenetic analysis of 16 Sec1p-related proteins from several species is consistent with the hypothesis that the evolution of this gene family parallels the specialization of vesicle trafficking to distinct intracellular compartments. By Northern analysis, each of these genes is expressed in all tissues examined (brain, spleen, lung, liver, skeletal muscle, kidney,

testis). While n-sec1 binds syntaxin 1a, 2, and 3, r-vps33a, r-vps33b and h-**vps45** do not bind any of the known syntaxins. We propose that the three proteins bind as yet unidentified syntaxin homologues involved in vesicle trafficking between the Golgi apparatus, prelysosomal compartment(s), and the lysosome.

L3 ANSWER 37 OF 41 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 95392039 MEDLINE
DOCUMENT NUMBER: 95392039 PubMed ID: 7663021
TITLE: Novel PI(4)P 5-kinase homologue, Fab1p, essential for normal vacuole function and morphology in yeast.
AUTHOR: Yamamoto A; DeWald D B; Boronenkov I V; Anderson R A; Emr S D; Koshland D
CORPORATE SOURCE: Carnegie Institution of Washington, Department of Embryology, Baltimore, Maryland 21210, USA.
CONTRACT NUMBER: GM-38906 (NIGMS)
GM-41718 (NIGMS)
GM-51968 (NIGMS)
+
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (1995 May) 6 (5) 525-39.
Journal code: BAU; 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U01017; GENBANK-X77395; GENBANK-X78998; GENBANK-Z22181
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951020
Last Updated on STN: 20000303
Entered Medline: 19951011

AB The FAB1 gene of budding yeast is predicted to encode a protein of 257 kDa that exhibits significant sequence homology to a **human** type II PI(4)P 5-kinase (PIP5K-II). The recently cloned **human** PIP5K-II specifically converts PI(4)P to PI(4,5)P2 (Boronenkov and Anderson, 1995). The region of highest similarity between Fab1p and PIP5K-II includes a predicted nucleotide binding motif, which is likely to correspond to the catalytic domain of the protein. Interestingly, neither PIP5K-II nor Fab1p exhibit significant homology with cloned PI 3-kinases or PI 4-kinases. fab1 mutations result in the formation of aploid and binucleate cells (hence the name FAB). In addition, loss of Fab1p function causes defects in vacuole function and morphology, cell surface integrity, and cell growth. Experiments with a temperature conditional fab1 mutant revealed that their vacuoles rapidly (within 30 min) enlarge to more than double the size upon shifting cells to the nonpermissive temperature. Additional experiments with the fab1 ts mutant together with results obtained with fab1 vps (**vacuolar protein sorting** defective) double mutants indicate that the nuclear division and cell surface integrity defects observed in fab1 mutants are secondary to the vacuole morphology defects. Based on these data, we propose that Fab1p is a PI(4)P 5-kinase and that the product of the Fab1p reaction, PIP2, functions as an important regulator of vacuole homeostasis perhaps by controlling membrane flux to and/or from the vacuole. Furthermore, a comparison of the phenotypes of fab1 mutants and other yeast mutants affecting PI metabolism suggests that phosphoinositides may serve as general regulators of several different membrane trafficking pathways.

L3 ANSWER 38 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:52459 BIOSIS
DOCUMENT NUMBER: PREV199698624594
TITLE: Characterization of three mammalian VPS33 and **VPS45** homologues implicated in Golgi to lysosome trafficking.
AUTHOR(S): Pevsner, J.
CORPORATE SOURCE: Kennedy Krieger Inst., 707 N. Broadway, Baltimore, MD 21205 USA
SOURCE: Molecular Biology of the Cell, (1995) Vol. 6, No. SUPPL., pp. 105A.
Meeting Info.: Thirty-fifth Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 9-13, 1995
ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 39 OF 41 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 94067128 MEDLINE
DOCUMENT NUMBER: 94067128 PubMed ID: 8246984
TITLE: Cloning of a novel, ubiquitously expressed **human** phosphatidylinositol 3-kinase and identification of its

binding site on p85.
AUTHOR: Hu P; Mondino A; Skolnik E Y; Schlessinger J
CORPORATE SOURCE: Department of Pharmacology, New York University Medical Center, New York 10016.
CONTRACT NUMBER: DK01927 (NIDDK)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1993 Dec) 13 (12) 7677-88.
Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19980206
Entered Medline: 19940103

AB Phosphatidylinositol 3-kinase (PI 3-kinase) has been implicated as a participant in signaling pathways regulating cell growth by virtue of its activation in response to various mitogenic stimuli. Here we describe the cloning of a novel and ubiquitously expressed **human** PI 3-kinase. The 4.8-kb cDNA encodes a putative translation product of 1,070 amino acids which is 42% identical to bovine PI 3-kinase and 28% identical to Vps34, a Saccharomyces cerevisiae PI 3-kinase involved in **vacuolar protein sorting**. **Human** PI 3-kinase is also similar to Tor2, a yeast protein required for cell cycle progression. Northern (RNA) analysis demonstrated expression of **human** PI 3-kinase in all tissues and cell lines tested. Protein synthesized from an epitope-tagged cDNA had intrinsic PI 3-kinase activity and associated with the adaptor 85-kDa subunit of PI 3-kinase (p85) in intact cells, as did endogenous **human** PI 3-kinase. Coprecipitation assays showed that a 187-amino-acid domain between the two src homology 2 domains of p85 mediates interaction with PI 3-kinase in vitro and in intact cells. These results demonstrate the existence of different PI 3-kinase isoforms and define a family of genes encoding distinct PI 3-kinase catalytic subunits that can associate with p85.

L3 ANSWER 40 OF 41 MEDLINE
ACCESSION NUMBER: 91358543 MEDLINE
DOCUMENT NUMBER: 91358543 PubMed ID: 1832167
TITLE: Dynamin: a microtubule-associated GTP-binding protein.
AUTHOR: Obar R A; Shpetner H S; Vallee R B
CORPORATE SOURCE: Cell Biology Group, Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545.
SOURCE: JOURNAL OF CELL SCIENCE. SUPPLEMENT, (1991) 14 143-5. Ref: 22
Journal code: HNG; 8502898. ISSN: 0269-3518.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911027
Last Updated on STN: 19911027
Entered Medline: 19911004

AB We recently identified dynamin as a third nucleotide-sensitive microtubule-associated protein in brain tissue, in addition to kinesin and cytoplasmic dynein. Molecular cloning analysis has revealed that dynamin contains the three consensus elements characteristic of GTP-binding proteins, and biochemical results support a role for GTP in dynamin function. Dynamin is also homologous to the Mx proteins, involved in interferon-induced viral resistance, and the product of the yeast VPS1 gene, involved in **vacuolar protein sorting**. These results identify a novel class of GTP-utilizing proteins, with apparently diverse functions.

L3 ANSWER 41 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1990:242809 BIOSIS
DOCUMENT NUMBER: BA89:129762
TITLE: A NEW CLASS OF LYSOSOMAL-**VACUOLAR PROTEIN SORTING** SIGNALS.
AUTHOR(S): KLIONSKY D; EMR S D
CORPORATE SOURCE: DIV. BIOL., CALIF. INST. TECHNOL., PASADENA, CA 91125.
SOURCE: J BIOL CHEM, (1990) 265 (10), 5349-5352.
CODEN: JBCHA3. ISSN: 0021-9258.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB A number of inherited lysosomal diseases are known to result from missorting of lysosomal proteins. Considerable attention has been directed

toward an understanding of this sorting pathway, and it has become apparent that different mechanisms are used for the sorting of lysosomal membrane and soluble proteins. Protein sorting to the yeast vacuole/lysosome provides a simple model system to study this processes. We have a mapped the first sorting signal in a vacuolar membrane protein, repressible alkaline phosphatase, and have shown it to be both necessary and sufficient for vacuolar delivery of this enzyme. The sorting information is confined to the transmembrane and cytoplasmic tail region of this type II integral membrane protein. The location of this sorting signal provides an explanation for some of the differences observed between membrane and soluble **vacuolar protein sorting**.

Set	Items	Description
S1	876	VACUOLAR(W)PROTEIN(W)SORTING
S2	145	VPS45
S3	79	S1 AND S2
S4	18	RD S3 (unique items)

?

09/566,178
DIALOG
Biochem
Biorci
Scott